

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Attorney Docket No.: **ISPH-0803**

Inventors: **Zhang and Watt**

Serial No.: **Not Yet Assigned**

Filing Date: **Herewith**

Examiner: **Not Yet Assigned**

Group Art Unit: **Not Yet Assigned**

Title: **Antisense Modulation of BCL2-Associated  
X Protein Expression**

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By *Jane Massey Licata*  
Typed Name: **Jane Massey Licata, Reg. No. 32,257**

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Sir:

**INFORMATION DISCLOSURE STATEMENT**

Pursuant to 37 C.F.R. §1.56 and in accordance with 37 C.F.R. §§1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 C.F.R. §1.56(b).

- (XX) In accordance with §1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in §1.491, or before the mailing date of a first Office Action on the merits of the above-identified application, no additional fee is required.
- ( ) In accordance with §1.97(c), this Information Disclosure Statement is being filed after the period set forth in §1.97(b) above but before the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311, therefore:
- ( ) Certification in Accordance with §1.97(e) is set forth below; or
- ( ) The fee of \$180.00 as set forth in §1.17(p) is attached.
- ( ) In accordance with §1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under §1.113 or a Notice of Allowance under §1.311 but before the payment of the Issue Fee, therefore included are: Certification in Accordance with §1.97(e); Petition Requesting Consideration of the Information Disclosure Statement; and the fee of \$130.00 as set forth in §1.17(I)(1).
- ( ) Copies of each of the references listed on the attached Form PTO-1449 (modified) are enclosed herewith.

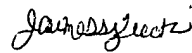
(XX) In accordance with §1.98(d), copies of some or all of the references listed on the attached Form PTO-1449 (modified) are not enclosed herewith because they were previously submitted to the U.S. Patent and Trademark Office in prior application Serial No. 09/908,147 filed July 17, 2001 for which a claim for priority under 35 U.S.C. §120 has been made in the instant application.

Please charge any deficiency or credit any overpayment to Deposit Account No. 50-1619. This form is submitted in duplicate.

( ) The relevance of the listed references in a foreign language is as stated in the specification at pages @@.

(XX) All listed references are in the English language.

Respectfully submitted,



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Date: December 5, 2003

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Form PTO-1449 Modified		Docket No. ISPH-0803	Serial No. not yet assigned
List of Patents and Publications Cited by Application (Use several sheets if necessary)		Applicant Hong Zhang et al.	
		Filing Date herewith	Group
U.S. Department of Commerce Patent and Trademark Office			
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	AA	Afford et al., <i>Apoptosis</i> , Mol. Pathol., 2000, 53:55-63	
	AB	Apte et al., Mapping of the human BAX gene to chromosome 19q13.3-q13.4 and isolation of a novel alternatively spliced transcript, BAX delta, <i>Genomics</i> , 1995, 26:592-594	
	AC	Brousset et al., Frequent expression of the cell death-inducing gene Bax in Reed-Sternberg cells of Hodgkin's disease, <i>Blood</i> , 1996, 87:2470-2475	
	AD	Chou et al., The BAX gene maps to the glioma candidate region at 19q13.3, but is not altered in human gliomas, <i>Cancer Genet. Cytogenet.</i> , 1996, 88:136-140	
	AE	Dibbert et al., Cytokine-mediated Bax deficiency and consequent delayed neutrophil apoptosis: a general mechanism to accumulate effector cells in inflammation, <i>Proc. Natl. Acad. Sci. U. S. A.</i> , 1999, 96:13330-13335	
	AF	Gillardon et al., Antisense oligodeoxynucleotides to bax mRNA promote survival of rat sympathetic neurons in culture, <i>J. Neurosci. Res.</i> , 1996, 43:726-734	
	AG	Isenmann et al., Bax antisense oligonucleotides reduce axotomy-induced retinal ganglion cell death in vivo by reduction of Bax protein expression, <i>Cell Death Differ.</i> , 1999, 6:673-682	
	AH	Knudson et al., Bax-deficient mice with lymphoid hyperplasia and male germ cell death, <i>Science</i> , 1995, 270:96-99	
	AI	Korsmeyer et al., Death and survival signals determine active/inactive conformations of pro-apoptotic BAX, BAD, and BID molecules, <i>Cold Spring Harb. Symp. Quant. Biol.</i> , 1999, 64:343-350	
	AJ	Korsmeyer et al., Pro-apoptotic cascade activates BID, which oligomerizes BAK or BAX into pores that result in the release of cytochrome c, <i>Cell Death Differ.</i> , 2000, 7:1166-1173	
EXAMINER		DATE CONSIDERED	

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		Filing Date herewith	Group
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	AK	MacGibbon et al., Bax expression in mammalian neurons undergoing apoptosis, and in Alzheimer's disease hippocampus, Brain Res., 1997, 750:223-234	
	AL	Manfredini et al., Antisense inhibition of Bax mRNA increases survival of terminally differentiated HL60 cells, Antisense Nucleic Acid Drug Dev., 1998, 8:341-350	
	AM	Oltvai et al., Bcl-2 heterodimerizes in vivo with a conserved homolog, Bax, that accelerates programmed cell death, Cell, 1993, 74:609-619	
	AN	Otter et al., The binding properties and biological activities of Bcl-2 and Bax in cells exposed to apoptotic stimuli, J. Biol. Chem., 1998, 273:6110-6120	
	AO	Park et al., Differential expression of Bax and Bcl-2 in the brains of hamsters infected with 263K scrapie agent, NeuroReport, 2000, 11:1677-1682	
	AP	Perez et al., Prolongation of ovarian lifespan into advanced chronological age by Bax-deficiency, Nat. Genet., 1999, 21:200-203	
	AQ	Podesta et al., Bax is increased in the retina of diabetic subjects and is associated with pericyte apoptosis in vivo and in vitro, Am. J. Pathol., 2000, 156:1025-1032	
	AR	Shi et al., Identification and characterization of baxepsilon, a novel bax variant missing the BH2 and the transmembrane domains, Biochem. Biophys. Res. Commun., 1999, 254:779-785.	
	AS	Tamatani et al., Involvement of Bcl-2 family and caspase-3-like protease in NO-mediated neuronal apoptosis, J. Neurochem., 1998, 71:1588-1596	
	AT	Tamatani et al., Growth factors prevent changes in Bcl-2 and bax expression and neuronal apoptosis induced by nitric oxide, Cell Death Differ., 1998, 5:911-919	
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	AU	Vila et al., Bax ablation prevents dopaminergic neurodegeneration in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine mouse model of Parkinson's disease, <i>Proc. Natl. Acad. Sci. U. S. A.</i> , 2001, 98:2837-2842	
	AV	Vukosavic et al., Bax and Bcl-2 interaction in a transgenic mouse model of familial amyotrophic lateral sclerosis, <i>J. Neurochem.</i> , 1999, 73:2460-2468	
	AW	Yel et al., Cartilage-hair hypoplasia syndrome: increased apoptosis of T lymphocytes is associated with altered expression of Fas (CD95), FasL (CD95L), IAP, Bax, and Bcl2, <i>J. Clin. Immunol.</i> , 1999, 19:428-434	
	AX	Yoshimura et al., Expression of bcl-2 and bax in glomerular disease, <i>Nephrol. Dial. Transplant</i> , 1999, 14:55-57	
	AY	Zhou et al., A novel splice variant of the cell death-promoting protein BAX, <i>J. Biol. Chem.</i> , 1998, 273:11930-11936	
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U.S. Department of Commerce Patent and Trademark Office	Filing Date	Group

**U.S. PATENT DOCUMENTS**

Examiner's Initial		Document No.	Date	Name	Class	Subclass
	AA	6,140,484	10/31/2000	Bitler et al.	536	23.1
	AB	5,691,179	11/25/1997	Korsmeyer	435	240.1
	AC	5,955,595	9/21/1999	Korsmeyer	536	23.5
	AD					
	AE					
	AF					
	AG					
	AH					
	AI					
	AJ					
	AK					
	AL					
	AM					
	AN					

**FOREIGN PATENT DOCUMENTS**

Examiner's Initial		Document No.	Date	Country	Translation YES NO	
	AO	WO 97/01635	01/16/1997	PCT	X	
	AP					
	AQ					
	AR					
	AS					
	AT					
	AU					
	AV					
	AW					
	AX					

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